UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,436	01/23/2002	Anne G. Byskov	4228.410-US	5453

23650 7590 11/18/2004

NOVO NORDISK, INC.
PATENT DEPARTMENT
100 COLLEGE ROAD WEST
PRINCETON, NJ 08540

EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/058,436	BYSKOV ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/448,217.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/12/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-22 are pending and under examination. Although the species election was not fully responded to, that is R1-R10 were not chosen and the claims readable thereon were not indicated as directed, in order to avoid more delay in the prosecution, the examiner has accepted the election of 4,4-dimethyl-5α-chloesta-8,14,24-trien-3β-ol as fulfilling the requirement.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11,17-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,645,953. Although the conflicting claims are not identical, they are not patentably distinct from each other because they claim common subject matter, as follows: methods of administration of a sterol with a 3-sulphonyloxy or phosphonyloxy moiety to regulate meiosis, *in vivo.*

Please note that the instant application is a CIP of several others and the claimed material has different dates of filing and the application and the patent cited above have one inventor in common, but different inventive entities and the same assignee.

Claims 1-11, 17-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5 and 6 of U.S. Patent No. 6,486,145. Although the conflicting claims are not identical,

they are not patentably distinct from each other because they claim common subject matter, as follows: methods of administration of a sterol with a 3-sulphonyloxy or phosphonyloxy moiety to regulate meiosis, *in vivo*.

Claims 1-11, 17-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-8 of U.S. Patent No. 6,407,086. Although the conflicting claims are not identical, they are not patentably distinct from each other because they claim common subject matter, as follows: methods of administration of a sterol with a 3-sulphonyloxy or phosphonyloxy moiety to regulate meiosis, *in vivo*.

Claim Rejections - 35 USC § 112

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for *in vivo* use. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

BREADTH OF THE CLAIMS

The claims are drawn to the use of hundreds of distinct sterols to regulate meiosis of male and female germ cells by *in vivo* administration.

STATE OF THE PRIOR ART AND NATURE OF THE INVENTION

The state of the prior art with regard to the administration of the claim specific sterols is a minimal or non-existent one. This appears to be a novel *in vivo* administration of 7 or 7,14 or 7,14,24 or 8, or 8,14 or 8,14,24-unsaturated sterols.

AMOUNT OF GUIDANCE AND WORKING EXAMPLES

The application states that 1-10g/day should be given to a mammal. Mammal is term which encompasses both elephants and mice. It is highly unlikely that if a dose of 1-10g/day is required for a mouse, that this dose would be effective in an elephant which has a body mass many fold larger than a mouse. According to the dose calculator @FDA.GOV, a 1 gram dose for a 0.02Kg mouse is equivalent to a dose of 3250 grams for a 65Kg human. There is clearly no teaching of effective dosages over the genus, mammals.

Also, metabolic precursors of cholesterol, such as 4,4'-dimethyl-5□-cholesta-8,14-dien-3□-ol, which is one of the sterols of formula I of the claims, would reasonably be expected to be metabolized to cholesterol when administered *in vivo* by metabolism in the liver. Please see Canonica *et al.* [U] for the metabolic fate of

the 8,14 dienes in mammals, which is conversion to cholesterol, an inactive sterol in the instant method. Therefore, little or no intermediate would be present in the blood and less even delivered to the target tissues. There appears to be no prior art directed to the administration of cholesterol intermediates to effect meiosis or any other biological function in intact animals. Neither is there is a working example of an *in vivo* administration of any sterol with an effect on any fertility parameter.

Further, only about 6 sterols, all with an 8,14 or 8-ene bond, are exemplified using oocytes *in vitro*. No 7-ene or 7,14-diene or 7,14,24-triene sterols have even been tested for activity *in vitro*.

UNPREDICTABILITY OF THE ART

As no evidence is of record that the use of all the sterols of formula I has a regulatory effect on meiosis, especially *in vivo*, and no evidence exists in the prior art of the administration of this class of sterols to intact animals, the unpredictability of the invention is extremely high. Predictability depends on prior experience. That which has never been known to occur before, cannot be predicted.

As set forth in *In re Fisher*, 427 F2.d 833, 839, 166 USPQ 18, 24 (CCPA) 1970: [Section 112] requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of the enablement varies inversely with the degree of unpredictability of the factors involved. *Ex parte Humphreys*, 24 USPQ2d, 1260.

Pharmaceutical therapies are unpredictable for the following reasons: (1) therapeutic compositions may be inactivated before producing an effect, i.e. such as proteolytic degradation of the peptide or protein; (2) the therapeutic composition may not reach the target area, i.e. the peptide or protein may not be able to cross the mucosa or may be adsorbed by fluids, cells and tissues where the peptide or protein has no effect, (3) other functional properties, known or unknown, may make the therapeutic composition unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. App. & Inter. 1992).

Although the specification discloses methods of administration of 8,14 and 8,14,24-enes *in vitro*, there are no data on the effectiveness of these sterols used

in a therapeutic treatment of a particular condition or to achieve regulation of a particular pathway in a particular target tissue in an intact animal. Therefore, in view of the nature of the invention, the state of the prior art, the amount of guidance present in the specification and the breadth of the claims, it would take undue experimentation to practice the claimed invention.

The claims encompass all mammals being treated with hundreds of distinct sterols. The amount of experimentation required to practice the claims over their breadth is not considered to be routine, but is considered to be undue because of the combination of the magnitude of the experimentation required and unpredictability in the art.

Claim Rejections - 35 USC § 102

Claims 1-3, 5, 11, 12, 19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Robbins *et al.* [IDS] or Zhikhar *et al.* [IDS] with Taylor *et al.* [IDS].

Robbins *et al.* disclose the administration of baker's or brewer's yeast to rats.

Zhikhar *et al.* disclose the administration of baker's yeast to rats.

Taylor *et al.* disclose that baker's yeast contains zymosterol.

Robbins *et al.* and Zhikhar *et al.* are the same one-step administration methods as claimed. As shown by Taylor *et al.*, yeast contain zymosterol, one of applicants claim specific sterols. Thus, the administration of yeast is the administration of zymosterol. Because the one-step method of administration to a mammal is the same and the amount of sterol, in the absence of evidence, appears to be the same as the claimed amounts, the results of the administration would reasonably be expected to be the same, that is, the regulation of meiosis in a germ cell. This would be an inherent result of the practice of the of the one step methods of the references.

Claims 1-11, 17-22 are rejected under 35 U.S.C. 103(a) as being obvious over US 6,645,953 or US 6,486,145 or US 6,407,086.

The applied reference US 6,645,953 has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any

invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, **at the time the invention was made,** owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

US 6,486,145 or US 6,407,086 do not have a common inventor. Therefore, the following rejection is applied.

Claims 1-11, 17-22 are rejected under 35 U.S.C. 102(f) over US 6,486,145 because the applicant did not invent the claimed subject matter.

Claims 1-10, 17-22 are rejected under 35 U.S.C. 102(f) over US 6,407,086 because the applicant did not invent the claimed subject matter.

US 6,645,953 or US 6,486,145 or US 6,407,086 teach a method of in vivo regulation of meiosis comprising administration of sterols with the 3 position having a phosphonyloxy or sulfonyloxy moiety.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sandra Saucier
Primary Examiner
Art Unit 1651